THE CATALYTIC HYDROGENATION OF ISOQUINOLINE AND 3-METHYLISOQUINOLINE

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THE CATALYTIC HYDROGENATION OF
ISOQUINOLINE AND 3-METHYLISOQUINOLINE

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ABSTRACT

A kinetic study has been made of the catalytic hydrogenation of isoquinoline and 3-methylisoquinoline using Adams' platinum catalyst and glacial acetic acid as the solvent. A standard Parr Hydrogenation Apparatus was employed in the reduction.

In the temperature range of 17 - 40° C. isoquinoline and 3-methylisoquinoline hydrogenate to the tetrahydro stage, where further hydrogenation does not occur. The rate of hydrogenation is zero order with respect to concentration of hydrogen acceptor, first order with respect to hydrogen pressure, and directly proportional to the amount of catalyst used.

The rate constant of the isoquinoline process has been determined to be 120×10^{-4} reciprocal minutes and that of the 3-methylisoquinoline process has been determined to be 243×10^{-4} reciprocal minutes with a catalyst that would hydrogenate benzoic acid under identical conditions at a rate of 250×10^{-4} reciprocal minutes in a system whose volume was 4.43 liters.

THE CATALYTIC HYDROGENATION OF ISOQUINOLINE AND 3-METHYLISOQUINOLINE

I. INTRODUCTION

Since aromatic nuclei are unusually resistant to reduction, catalysts must be employed in hydrogenation work carried out in the laboratory. By the use of such catalysts as nickel, copper chromite, and platinum it is possible not only to synthesize new compounds, but also to make kinetic studies from acquired reaction rates.

Of the earlier methods of reducing aromatic compounds, platinum was used in the form of platinum black or colloidal platinum.[1,2,3,4] These methods required large amounts of catalyst and long intervals of time for reduction of small amounts of a compound; therefore, they were not practical.

In 1922, Adams and co-workers found that platinum oxide had the ability to reduce aromatic nuclei better than any other

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[1] R. Willstatter and D. Hatt, Ber., 45, 1471 (1912).

[2] R. Willstatter and E. Waldschmidt-Leitz, Ber., 54, 113 (1921).

[3] A. Skita and W. A. Meyer, Ber., 45, 3589 (1912).

[4] A. Skita and W. A. Meyer, Ber., 55, 144 (1922).

catalyst.[5,6,7] The reductions carried out with this catalyst required only room temperature and three to four atmospheres pressure of hydrogen with the material to be hydrogenated dissolved in glacial acetic acid.

Although much research has been made on the catalytic reduction of aromatic compounds, there had been little work done on reaction rates or kinetics of these reductions until 1945. At that time H. A. Smith and co-workers, under essentially the same conditions as Adams and co-workers, made a kinetic study of the reduction of phenyl-substituted aliphatic acids.[8] Investigations of this character have been extended to include hydrogenations of benzene, the mono-alkylbenzenes, and the polymethylbenzenes, and other hydrogen acceptors.[9,10]

It has been concluded from these kinetic studies on the hydrogenation of the benzene nucleus that:

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[5]R. Adams and J. Marshall, J. Am. Chem. Soc., 50, 1970 (1928).

[6]R. Adams and R. L. Shriner, J. Am. Chem. Soc., 45, 2174 (1923).

[7]R. Adams, R. L. Shriner, and V. Voorhees, Organic Synthesis, Coll. Vol. I, (New York: John Wiley and Sons, Inc., 1932). p. 463.

[8]H. A. Smith, D. M. Alderman, and F. W. Nadig, J. Am. Chem. Soc., 67,272 (1945).

[9]H. A. Smith and E. F. H. Pennekamp, J. Am. Chem. Soc., 67, 276 (1945).

[10]Ibid., p. 279.

1. The reaction is zero order with respect to the concentration of the compound being hydrogenated;
2. The rate is directly proportional to the amount of catalyst used;
3. The reaction rate is first order with respect to hydrogen pressure;
4. The phenyl group is strongly adsorbed on the catalyst while the other portions of the molecule are not;
5. Resonance is not a factor which influences greatly the reaction rate;
6. The symmetry of the molecule is an important factor in determining the reaction rate.

More recent studies have extended the investigation to pyridine.[11] Stanfield, Trimble, and Hecht included studies on quinoline.[12,13] The same conclusions as above were given with the exception that in the case of pyridine two modifications were necessary:

1. There was a slight dependence of the reaction rate on the concentration of the hydrogen acceptor;

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[11]J. A. Stanfield, "Kinetics of Catalytic Hydrogenation," Doctoral Dissertation, University of Tennessee, 1947. Part B.

[12]A. T. Trimble, "The Catalytic Hydrogenation of Quinoline," Master's Thesis, Georgia Institute of Technology, 1949.

[13]J. L. Hecht, "The Catalytic Hydrogenation of Quinolines," Master's Thesis, Georgia Institute of Technology, 1950.

the smaller the concentration of pyridine, the greater was the rate constant.

2. The reaction rate is first order with respect to hydrogen pressure over a small pressure range, and over greater pressure differences it was calculated to be 0.98 order.

It is the purpose of this investigation to test the validity of previous conclusions, as given above, when applied to isoquinoline and 3-methylisoquinoline. At the present a kinetic study of these compounds as hydrogen acceptors has not been made.

II. THEORETICAL DISCUSSION

All chemical reactions take place at a definite rate or speed whether they occur so rapidly that they appear to be instantaneous or whether they are so slow that there is no detectable change. Between these extremes there are reactions which take place at velocities which may be easily measured in the laboratory. The reaction rates depend upon certain conditions, the most important of which include concentration of reactants, temperature, volume, pressure, and amount of catalyst present. It is the study of the reaction rates and the influence of the conditions on these rates that is included in a study of chemical kinetics.

A. Chemical Kinetics

1. Reaction Rates.

Since chemical reactions proceed at definite rates, it is possible to express the relation of reaction rate with concentration by mathematical expressions. In reactions where the rate is proportional to the concentration of none, one, or two of the reactants, simple standard expressions can be obtained. However, in many processes there are two or more reactions taking place at the same time so that the mathematical treatment of the over-all reaction is very complex. This study will not include a discussion of complex reactions, but

will be limited to the simple orders which are used in elementary expressions.

The order of a reaction with respect to a given reactant indicates the exponent to which the concentration of the reactant must be raised in the expression for the reaction rate. It is only with two of these orders that this paper is concerned--zero and first orders.

The zero order reaction, first of the reaction orders which can be expressed in a simple manner, is unaffected by the concentration of the reactants.[1] The rate is determined by some limiting factor such as the absorption of light in certain photochemical reactions, or the rate of diffusion in certain surface reactions. In reactions of this order the rate of change in concentration of the substance is given by the expression

$$-\frac{dc}{dt} = k, \qquad (1)$$

where c is the concentration, t is the time, and k is the proportionality constant, or the "rate constant" of the reaction. By integration of equation (1) it is possible to evaluate the constant experimently, which is shown by equations (2) and (3).

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[1] F. Daniels, Outlines of Physical Chemistry, (New York: John Wiley and Sons, Inc., 1948). p. 353.

$$-\int_{c_1}^{c_2} dc = k \int_{t_1}^{t_2} dt \qquad (2)$$

$$c_2 - c_1 = -k\,(t_2 - t_1) \qquad (3)$$

Smith and co-workers observed zero order dependence when investigating the effect of concentration of hydrogen acceptor upon the rate of the hydrogenation of benzene and monoalkylbenzenes, the polymethylbenzenes, and phenyl-substituted aliphatic acids.

The first order reaction is the second of the simple order expressions to be discussed in this study. It is one in which the rate is directly proportional to the concentration of one of the reacting substances.[2] The condition can be expressed mathematically in the form

$$-\frac{dc}{dt} = kc, \qquad (4)$$

which states that the rate of disappearance of the reactant at any instant is proportional to its concentration at that instant.

Integration of equation (4) between limits gives

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[2]F. Daniels, op. cit., p. 345.

$$-\int_{c_1}^{c_2} \frac{dc}{c} = k \int_{t_1}^{t_2} dt \tag{5}$$

$$-\ln c_2 + \ln c_1 = k\,(t_2 - t_1) \tag{6}$$

$$\log \frac{c_1}{c_2} = \frac{k}{2.303}\,(t_2 - t_1), \tag{7}$$

where at time t_1 the concentration is c_1, and at time t_2 the concentration is c_2.

Equations (3) and (7) apply to a general case of zero order and first order reactions. For this work they may be simplified by replacing c_1 by c_o, the initial concentration; c_2 by c, the final concentration; t_1 by 0, the initial time; and t_2 by t, the final time. The more useful equations obtained are:

$$c_o - c = kt \tag{8}$$

$$\log \frac{c_o}{c} = \frac{kt}{2.303} \tag{9}$$

In a case wherein the reactant is a gas, since the pressure of the gas is proportional to its concentration, pressures may be substituted for concentrations. When c_o is replaced by p_o, the initial pressure, and c by p, the final pressure, the first order rate equation obtained from equation (9) becomes

$$\log \frac{p_o}{p} = \frac{kt}{2.303} \qquad (10)$$

Equation (10) for a first order reaction is very useful for determining rates in some catalytic hydrogenations, for which the rates have been found to be first order with respect to the hydrogen pressure. After taking pressure readings at definite time intervals, a plot of log (p_o/p) against t is made. A straight line of slope k/2.303 may be obtained and from this k is readily calculated. As an example of this, the rate of hydrogenation of methyl-substituted benzoic acids was found to be first order with respect to the hydrogen pressure.[3]

2. Factors Influencing the Reaction Rate Constant.

When such factors as temperature and volume are altered in the investigation of reaction rates, it should be expected that the proportionality constant will vary. Therefore, the variables which affect the reaction rate constant should be considered.

a. Temperature. An increase in temperature practically always increases the rate of reaction. In homogeneous reactions, the rate is doubled, or even trebled, for each ten-degree rise in temperature. Arrhenius found empirically that the variation

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[3]J. A. Stanfield, "Kinetics of Catalytic Hydrogenation," Doctoral Dissertation, University of Tennessee, 1947. p. 29.

of the reaction rate constant k with temperature in both homogeneous and heterogeneous reactions may be expressed by

$$\frac{d \ln k}{dT} = \frac{E_a}{RT^2} , \qquad (11)$$

where k, T, and R have their usual meaning and E_a is an energy quantity known as the "energy of activation" or "heat of activation."[4] Upon integration of equation (11), there is obtained the following:

$$\ln k = - \frac{E}{RT} + \text{constant} \qquad (12)$$

$$\log k = - \frac{E}{2.303RT} + \text{constant} \qquad (13)$$

According to equation (13), if a plot of log k against 1/T is made, a straight line is obtained which has a slope which equals -E/2.303R. The value of E_a is then calculated by multiplying the slope by -2.303R.

If a straight line is not obtained from the plot of log k against 1/T, it may be an indication that the reaction is made up of two or more concurrent reactions, which are differently influenced by temperature.[5] Pyridine and methyl-substituted pyridines have been observed to have two activation

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[4]S. Glasstone, Textbook of Physical Chemistry, 2nd Edition, (New York: D. Van Nostrand, Inc., 1946). p. 1088.

[5]C. N. Hinshelwood, The Kinetics of Chemical Change in Gaseous Systems (Oxford: Oxford University Press, 1940). p. 45.

energies.[6]

The energy of activation is useful not only from a theoretical standpoint, but from a practical standpoint. The Arrhenius equation may be used to convert rate constants determined at one temperature to any other temperature within the range of which the energy of activation is applicable. In order to obtain the equation in a more useful form, equation (11) is integrated as follows:

$$\int_{k_1}^{k_2} d \ln k = \frac{E_a}{R} \int_{T_1}^{T_2} \frac{dT}{T^2} \tag{14}$$

$$\ln \frac{k_2}{k_1} = - \frac{E_a}{R} \left(\frac{1}{T_2} - \frac{1}{T_1}\right) \tag{15}$$

$$\log \frac{k_2}{k_1} = - \frac{E_a}{2.303R} \left(\frac{1}{T_2} - \frac{1}{T_1}\right). \tag{16}$$

When the values for the energy of activation and k_1 at T_1 are known, the value for k_2 at T_2 may be calculated.

b. Volume. It has been shown by Fuzek and Smith that the rate constant is dependent upon the volume of the gaseous system employed.[7] They showed that the product of

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[6]Stanfield, op. cit., p. 84.

[7]J. F. Fuzek and H. A. Smith, "Kinetics of Heterogeneous Reactions with Special Reference to Catalytic Hydrogenation," J. Am. Chem. Soc., 70, 3743 (1948).

the rate constant times the volume does not change. This may be shown by considering two reactions involving a gaseous reactant, e.g., hydrogen.

On assuming that the gas acts ideally and that each reaction occurs at constant volume, at the same temperature and at the same initial pressure, the decrease in energy associated with the reactions may be formulated as:

$$P_1V_1 - P^oV_1 = n_1RT - n_1^oRT \tag{17}$$

$$P_2V_2 - P^oV_2 = n_2RT - n_2^oRT, \tag{18}$$

where P^o, n_1^o, and n_2^o represent the initial states, and P_1, n_1, P_2, and n_2 represent the final states.

The equations may be rewritten as:

$$V_1dP_1 = RTdn_1 \tag{19}$$

$$V_2dP_2 = RTdn_2, \tag{20}$$

when the changes made are infinitesimal. When the reactions are permitted to proceed at a time dt such that dn_1 is equal to dn_2, they may be expressed as:

$$V_1dP_1 = V_2dP_2. \tag{21}$$

A first order reaction with respect to the pressure of a reactant is expressed in the following manner:

$$-\frac{dP}{dt} = kP. \tag{22}$$

At the time P is equal to P^o, for the two reactions equation (22) may be written:

$$dP_1 = - k_1 P^o dt \qquad (23)$$

$$dP_2 = - k_2 P^o dt \qquad (24)$$

By combining equations (21), (23), and (24), the expressions obtained are:

$$V_1 k_1 = V_2 k_2 \qquad (25)$$

$$Vk = \text{a constant} \qquad (26)$$

Therefore, whenever the volume of a gaseous system is changed, conventional rate equations must be modified.

B. Catalytic Hydrogenation

The chemical addition of hydrogen to a compound in the presence of a catalyst is known as catalytic hydrogenation. The substance to be hydrogenated is brought into contace with hydrogen and finely divided metals, oxides, or a fixed catalytic surface at a proper temperature. If the reactants and the catalyst are physically of the same state and phase, the process is known as homogeneous catalysis; and, if the catalyst and the reacting and resulting substances are in different phases, it is known as heterogeneous catalysis.[8]

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[8]H. W. Lohse, Catalytic Chemistry (New York: Chemical Publishing Company, 1945). pp. 59 and 81.

Adkins has listed the following requirements for a good catalyst for hydrogenation: It must

(1) be stable in the presence of the reactants;

(2) adsorb and activate hydrogen;

(3) adsorb and activate the hydrogen acceptor;

(4) hold the activated hydrogen and hydrogen acceptor; in the proper relationship for reaction;

(5) desorb or set free the reaction product (s).[9]

Certain aspects of catalytic hydrogenation should be considered in order to elucidate the utilization of the catalyst; they are adsorption, promotion, poisoning and selectivity.

1. Adsorption.

The three types which should be considered in order to obtain an understanding of adsorption are: (1) physical adsorption, (2) activated adsorption, and (3) chemisorption.[10] The first type takes into consideration the adsorption of a gas or vapor by a solid at low temperature where the adsorption is completely reversible and equilibrium is rapidly attained. Activated adsorption occurs at a higher temperature than the physical case, and equilibrium is reached more slowly. The third type, chemisorption, is due to formation of a chemical compound between an adsorbed material and a contact surface.

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[9]H. Adkins, Reactions of Hydrogen With Organic Compounds over Copper-Chromium Oxide and Nickel Catalysts (Madison: The University Press, 1937). p. 9.

[10]Lohse, op. cit., p. 83

A mere physical adsorption of gases, vapors, and liquids, on contact surfaces of no specific chemical activity is not enough to induce chemical activity. In order for the contact surface to become chemically reactive, it must possess those specific properties which are embodied in the activity of the catalyst. This property is specific for the catalytic reaction in question. The adsorption of the reactants on a catalytically active contact surface is of great importance because it is in this manner the reactants are brought close together and in proper spatial position. Therefore, for high catalytic activity the catalyst must actively adsorb the reactants, and in order to maintain its activity, it must not have a very great affinity for the products of the reaction.

2. Promoters and Poisons.

The action of a catalyst may be influenced greatly by the presence of a variety of materials, though they be present in small quantities. A promoter is a substance, which does not act catalytically when used alone, but on its addition to a catalyst increases the catalytic action. A summary on the assumptions and proposals for promoter action has been made by Weiser.[11] He states that a promoter may

1. act by increasing the number of active centers as a result of an increase in the number of crystal faces, edges, and corners on the catalytic surface;

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[11] H. B. Weiser, Colloid Chemistry (New York: John Wiley and Sons, Inc., 1946). p. 51.

2. furnish an interface at which adsorption takes place;
3. increase the velocity of activated adsorption;
4. change the ratio of adsorption of two reacting substances;
5. activate one of the reacting substances which the catalyst did not activate appreciably;
6. decrease the stability of an intermediate product;
7. decrease the adsorption of one of the products below the point at which it has a poisoning action;
8. modify the nature of the orientation of the catalyst crystals.

A substance in a minute quantity that possesses the property of partly or wholly destroying the activity of a catalyst is known as a poison. Although catalyst poisons are usually thought of as hindering positive catalysis, they can be useful in that they may repress undesirable reactions.

3. Selectivity.

The selectivity of the catalyst is of great importance in catalytic reactions. This is shown by the fact that in hydrogenations nickel is more active with respect to carbon-to-carbon double bonds than it is to carbon-to-oxygen double bonds; whereas, copper chromite is more active toward carbon-to-oxygen double bonds than to carbon-to-carbon double bonds.[12]

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[12]Lohse, op. cit., p. 95

Although the selectivity of a catalyst seems to depend greatly upon the catalyst itself, it may be changed by altering the conditions of the reaction. Some of these conditions are temperature, solvent, if any, duration of the reaction, and pressure, if gaseous, or concentration of the reacting species.

III. EXPERIMENTAL

In the course of an investigation such as this, care should be shown in the selection of equipment, materials, and procedures in order that the results be significant. Since these factors may influence the results, it is appropriate to give a summary of them.

A. Equipment

In this research the reductions were carried out in a standard low-pressure hydrogenation apparatus, manufactured by the Parr Instrument Company of Moline, Illinois. This consisted of the following: to a four liter, cylindrical, metal tank was attached a pressure gauge and suitable valves connecting one end to a source of hydrogen and connecting the other end to a reaction bottle. A 400 ml. reaction bottle was fitted with a copper connection having a treated rubber stopper. Throughout this work a brass, water-tight, cylindrical jacket, constructed in this laboratory, surrounded the reaction bottle. By use of a centrifugal pump water was circulated around the reaction bottle from a large water reservoir, equipped with a stirrer. A shaking device driven by a one-sixth horsepower electric motor was employed to bring about agitation of the reaction vessel. Thus, the reductions were carried out at a desired constant temperature.

The Parr pressure gauge was replaced by a mercury manometer when hydrogenations were run at an initial pressure of around sixteen p.s.i.

B. Materials

1. Catalyst.

The same platinum oxide catalyst (81.76% Pt), prepared by the American Platinum Works, Newark, New Jersey, was used throughout this work.

2. Hydrogen.

Hydrogen was obtained from the National Cylinder Gas Company, Atlanta, Georgia, and was used without further purification.

3. Acetic Acid.

The glacial acetic acid, c. p., sold by duPont, was purified by distillation through a five-foot column packed with glass helices and having about 40 theoretical plates. The acetic acid, boiling at a constant temperature of 115.8° C. at 740 mm. (corrected), was collected at a reflux ratio of 10:1.[1] It was found sufficiently pure to be used as a solvent for the hydrogen acceptor.

4. Benzoic Acid.

Benzoic acid, c. p., used in determining the catalyst factor, was obtained from the Merck Chemical Company, Rahway, New Jersey. It was used without further purification.

5. Isoquinoline.

After the careful purification of Eastman Kodak practical grade isoquinoline, the same sample was used throughout

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[1]Anschutz thermometers were used consistently in the distillations and no corrections were applied.

this study. The isoquinoline was first cooled to 0° C. and then filtered through an ice-cooled Buechner funnel to remove any quinoline impurities present. (The freezing point of quinoline is -19.5° C. and that of isoquinoline is 23.0° C.) The isoquinoline filtrate was then allowed to remain at room temperature over sodium hydroxide pellets for three weeks.

The hydrogen acceptor was then decanted and distilled through a six-foot Vigreux column of approximately 23 theoretical plates. The distillation was carried out in an atmosphere of dry nitrogen to prevent possible contamination from oxygen and moisture. Small particles, presumably charcoal, were filtered from the nitrogen by passing the nitrogen through a glass tube filled with glass wool. That fraction boiling at a constant temperature of 240.0° C. at 737 mm. (corrected) was collected at a reflux ratio of 10:1. The isoquinoline was stored in the dark in a small bottle under an atmosphere of nitrogen until it was needed for use.

6. 1,2,3,4-Tetrahydroisoquinoline.

1,2,3,4-tetrahydroisoquinoline was obtained as the hydrogenated product of isoquinoline. After the spent catalyst had been removed most of the acetic acid was removed by distillation under reduced pressure, and that remaining was rendered basic with 20% sodium hydroxide. This tetrahydroisoquinoline was extracted with anhydrous diethyl ether. It was finally distilled through the same column and in a like

manner as was the isoquinoline. That fraction at a constant boiling temperature between 133.9 - 134.1° C. at 739 mm. (corrected) was collected and stored under an atmosphere of nitrogen until it was ready to be hydrogenated.

7. 3-Methylisoquinoline.

Because there are so few references in the literature to 3-methylisoquinoline, the purity of this product was determined through its melting point, 64.7° C. This organic compound was recrystalized from anhydrous diethyl ether and ligroin (90° - 120° C., Eastman Kodak Company, Rochester, New York). The 3-methylisoquinoline was dissolved in the ligroin, filtered through charcoal, and the ligroin was evaporated. This procedure was repeated from eight to ten times--until the compound was perfectly white--and the white product was dried in an oven at 55.0° C. for forty-eight hours. The melting point was found to be 64.5° C. It was then stored until it was ready for hydrogenation.

C. Procedure

1. Preparation Before Hydrogenation Procedure.

It was essential that the apparatus be absolutely clean in order that results obtained might be both accurate and reproducible. The reaction bottles, first washed with soap and rinsed with water, were filled with cleaning solution, then let to stand for thirty minutes. After rinsing several times, first with tap water and then with distilled water, the

bottles were dried at least three hours in an oven at 110° C. Using an analytical balance the catalyst samples of benzoic acid and 3-methylisoquinoline were weighed out on a tared watch glass to the nearest 0.2 mg. The isoquinoline samples of 0.01 mole to 0.04 mole were measured by means of a calibrated pipette with suitable connections for carrying this out in an atmosphere of nitrogen.[2] 50 ml. of acetic acid, measured in a 100 ml. graduated cylinder, was used in all the hydrogenations.

The water reservoir was brought to the desired temperature by adding ice or hot water. This temperature was maintained with an accuracy of ± 1.0° C.

It was imperative that the rubber stopper, which fitted on the brass connection tube from the reaction bottle to the hydrogen tank, be clean. The stopper was washed with water, boiled for thirty minutes in 20% sodium hydroxide, washed, and boiled again in distilled water. The treatment was completed by a final washing in distilled water and drying.

The brass connection tube just mentioned was cleaned before and after each hydrogenation with pipe cleaners moistened with methanol. If this were not done, there would be a poisoning of the catalyst.

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[2] J. L. Hecht, "The Catalytic Hydrogenation of Quinolines," Master's Thesis, Georgia Institute of Technology, 1950.

2. Hydrogenation Procedure.

Since all the hydrogenations were carried out at constant temperature, the acetic acid was initially added to the reaction bottle and both put in the water jacket until the solvent reached the temperature of the water. A weighed or pipetted sample and then the catalyst were added immediately before inserting the reaction vessel in position. The vessel was then evacuated with a Cenco-Hyvac pump until the acetic acid began to boil. When this point was reached, the proper valve was closed and hydrogen gas was permitted to flow from the gas tank to the reaction bottle. This was repeated two more times to insure the removal of all the air in the system. After the third evacuation the system was charged with hydrogen from the gas cylinder until the gauge pressure read 50 p.s.i., that is, all runs except those made at 32 and 16 p.s.i. (absolute pressure). At the latter pressure, a manometer was used. As soon as the shaking began, the time, determined with a precision stop watch, was recorded. The interval of time between each reading of the drop in hydrogen pressure, which could be read to an accuracy of ± 0.1 pound, was determined by the rate of hydrogenation; the usual time interval was two minutes.

After the hydrogenation was completed, the valve connecting the reaction bottle and the gas cylinder was closed. By opening the proper valve the hydrogen in the bottle was

allowed to escape, and this part of the system was evacuated before permitting the air to flow back into the system up to the gas tank. The reaction flask was removed, and the contents were filtered through a sintered glass funnel to separate the spent catalyst from the hydrogen acceptor and acetic acid. The hydrogenation apparatus was left evacuated until the next hydrogenation.

3. Isolation of Products.

After the removal of the spent catalyst from the hydrogenated compound, the acetic acid was removed by distillation under reduced pressure. The remaining portion was rendered basic with 20% sodium hydroxide and extracted with benzene or diethyl ether. Final purification was effected by distillation through a fractionating column, in some cases under reduced pressure and in others under atmospheric pressure.

IV. DISCUSSION OF RESULTS

A. Determination of Rate Constant

1. Basis of Interpretation.

Since there are a number of variables which greatly influence the rate of reaction, it is necessary to adopt certain standard conditions. Therefore, on the basis of interpretation of previous work and preliminary runs with isoquinoline, analyses of the experimental results permitted a kinetic study to be made. The individual factors which serve as this basis of interpretation are as follows:

a. Smith, Alderman, and Nadig, in their work on the benzene nucleus, defined a standard catalyst as one whose rate constant for the hydrogenation of benzoic acid was 250×10^{-4} reciprocal minutes, for one gram of catalyst at 30.0° C. in 50 ml. of acetic acid under an initial hydrogen pressure of 64 pounds per square inch.[1] In a like manner, a standard reaction rate constant of a reaction, K° was defined as the rate constant of a given reaction corrected to 30.0° C. and one gram of catalyst, and multiplied by a "catalyst factor" to bring all catalysts to the same basis.

b. As illustrated in Figures 1, 2, and 4, an induction period of one to three minutes--even up to six minutes

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[1] H. A. Smith, D. M. Alderman, and F. W. Nadig, J. Am. Chem. Soc., 67, 272 (1945).

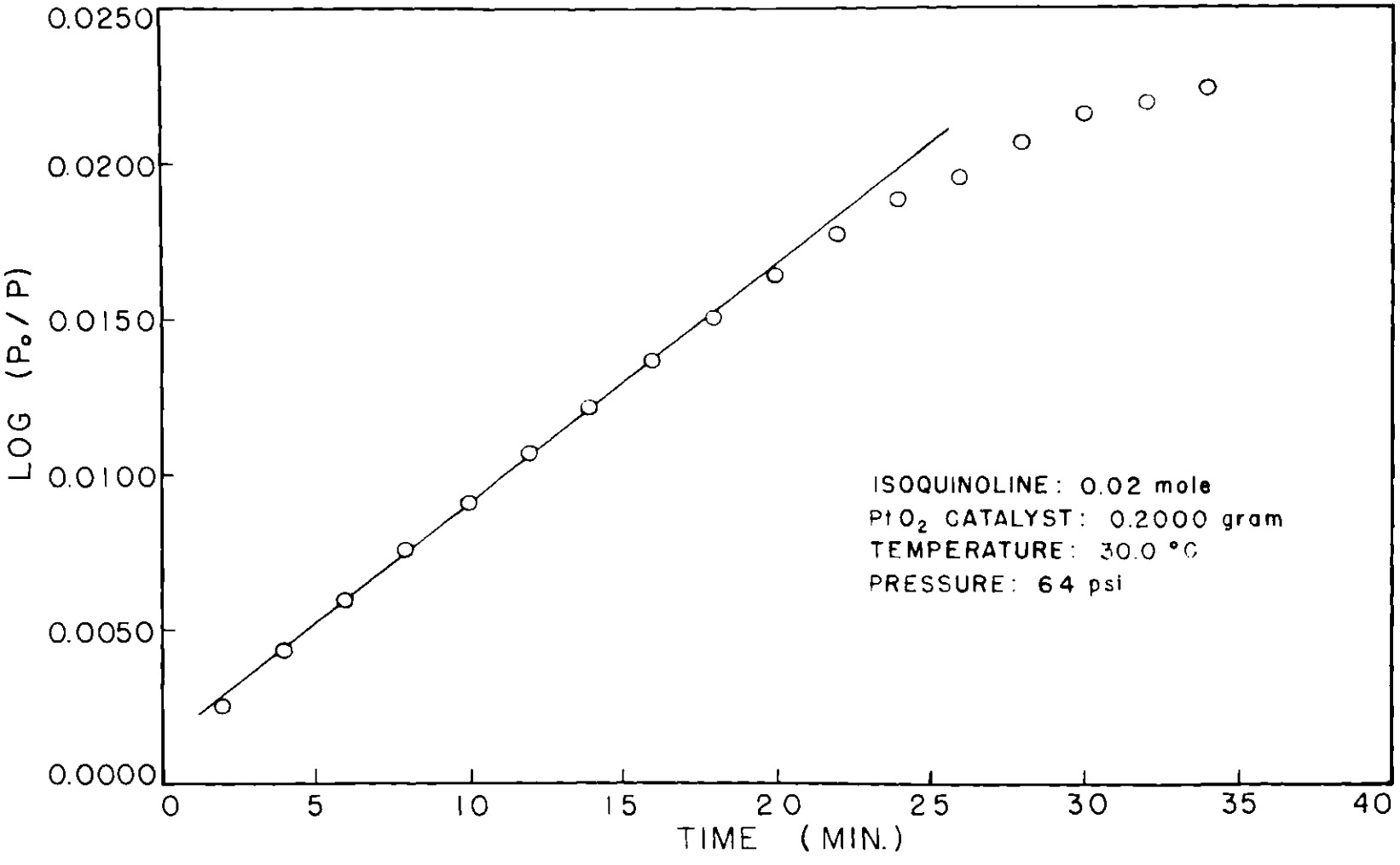

FIGURE 1

SAMPLE HYDROGENATION CURVE FOR ISOQUINOLINE

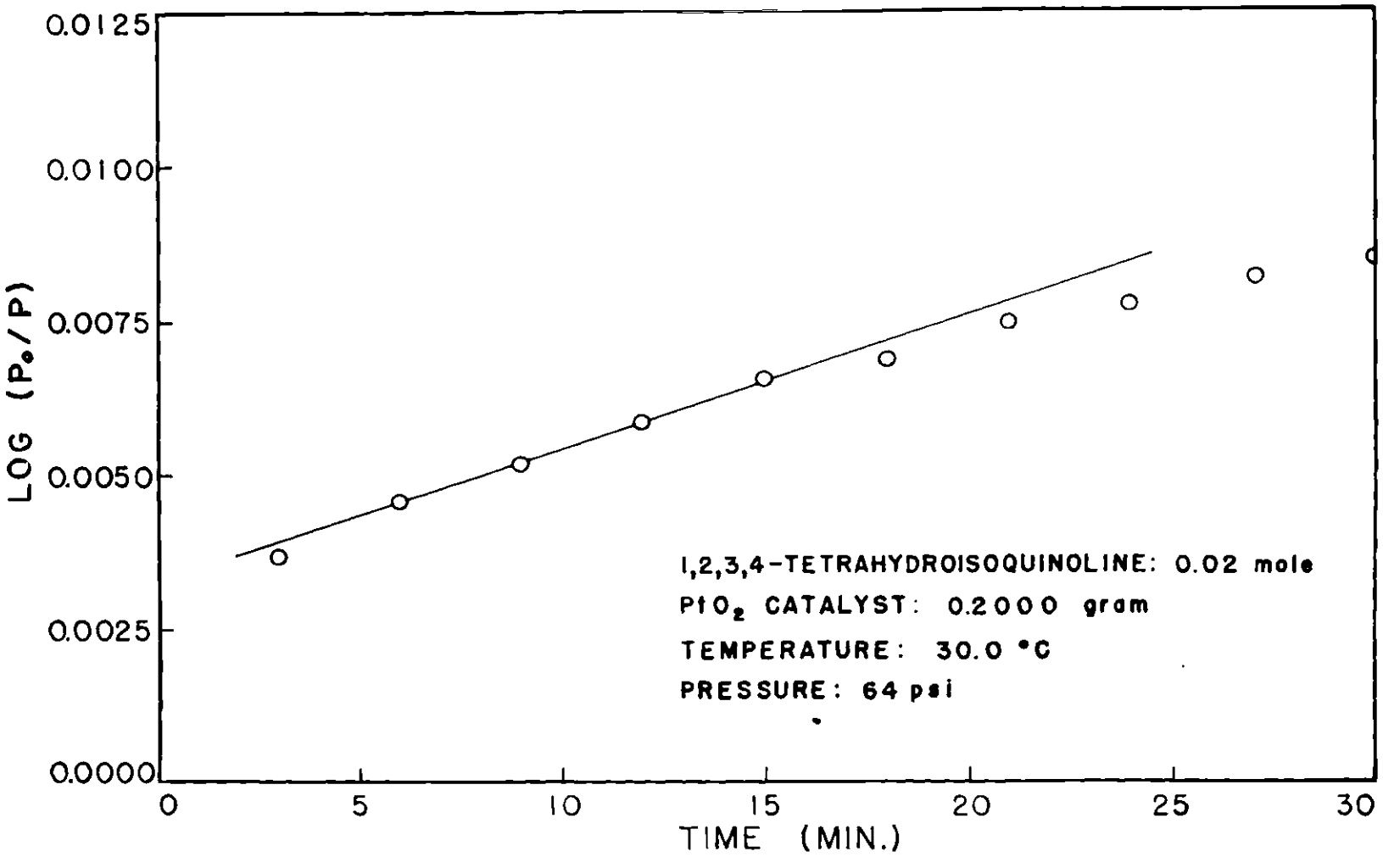

FIGURE 2

SAMPLE HYDROGENATION CURVE FOR
1,2,3,4-TETRAHYDROISOQUINOLINE

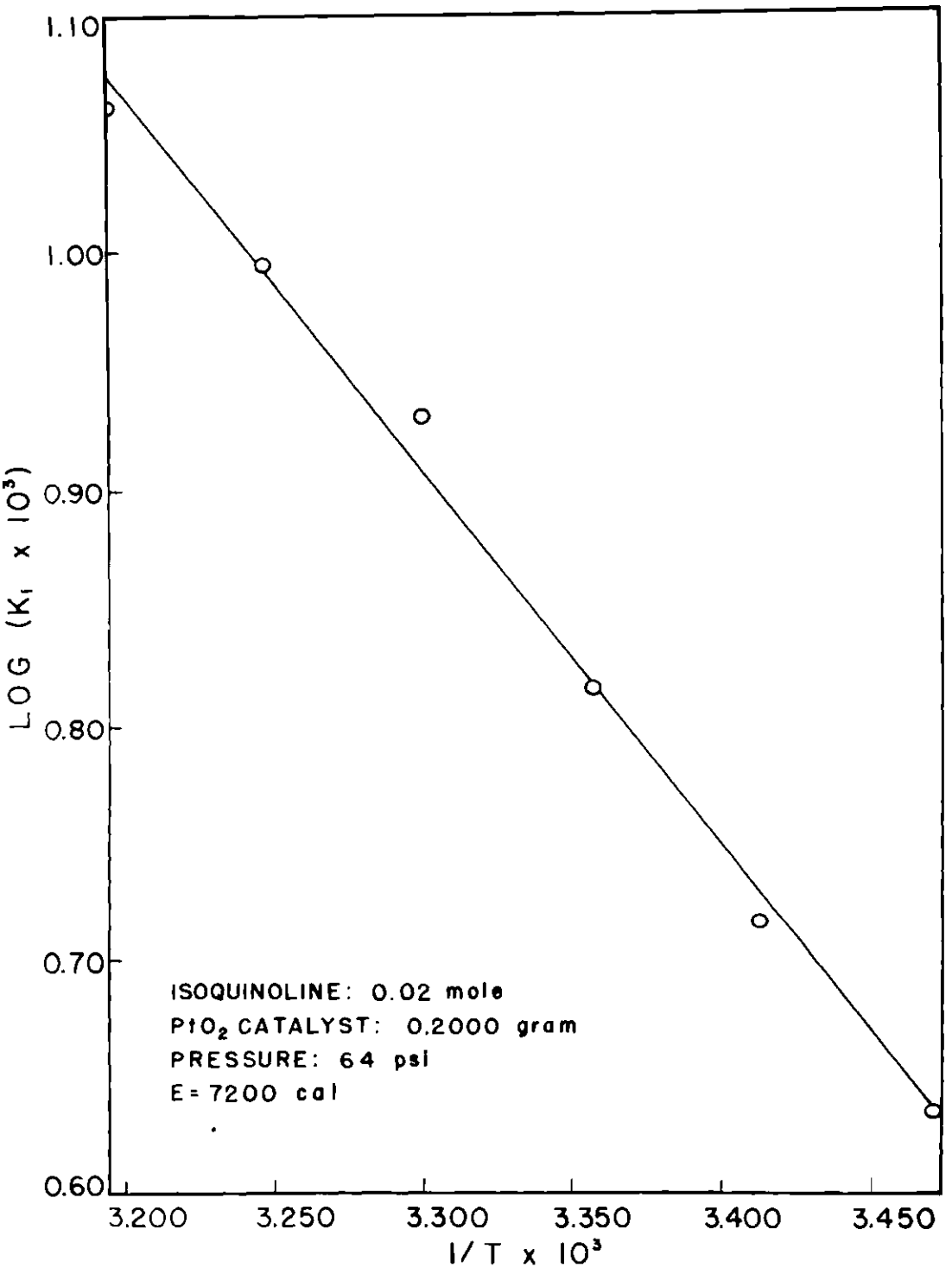

FIGURE 3

ENERGY OF ACTIVATION FOR THE HYDROGENATION OF ISOQUINOLINE

in some hydrogenations, where the rate constant is small--has been postulated. This has been attributed to the reduction of the platinic oxide catalyst to platinum and platinum oxides, which actually serve as the catalyst.

c. Near the end of each hydrogenation, as shown in Figures 1 and 4, there was a gradual slowing down of the reaction; this was thought to be due to poisoning. As this effect did occur in the hydrogenation of benzoic acid and quinoline, it seems as if this same factor might be accounted for in this work. This poisoning is probably due in part to the slight adsorption of the hydrogenated product, thus decreasing the amount of surface available for the hydrogen acceptor.

2. Standard Rate Constant.

The standard hydrogen acceptor selected was benzoic acid, because: it supplied a benzene nucleus; it could be used as purchased without further purification; its rate of hydrogenation was zero order with respect to concentration; and, its rate of change of hydrogen pressure at the given temperatures was such that it could be observed with reasonable accuracy on the Parr hydrogenation apparatus.

Since the same catalyst was used throughout this investigation, the catalyst factor has only been used in the sample calculation of the standard reaction rate constant, p. 33, where its value is given. This factor was obtained

by dividing 250 x 10^{-4} by the experimentally determined rate constant for the hydrogenation of benzoic acid, 182.5 x 10^{-4}. Therefore, in order for the rate constants, K_{30^o}, in this thesis to be compared with the standard rate constant, $K^o_{30^o}$ in other investigations, all that is necessary is to multiply K_{30^o} by the catalyst factor.

It was not necessary to correct for the acetic acid volume and hydrogen volume since they remained constant throughout the work. The initial hydrogen pressure was approximately 64 pounds per square inch in all runs reported except where a study was made of the effect of initial hydrogen pressure, illustrated in Table VI, p. 40. In all reductions except those noted in Tables IV and V, 39, where a study was made on the effect of varying the amount of catalyst, 0.2000 gram of catalyst was used; a factor was employed in order to interpret the results on a 1.0000 gram catalyst basis. Except in Tables I and II, p. 36, 0.02 mole hydrogen acceptor was used. Equation (16), p. 11, was employed in determining the energy of activation and was used when the reaction was run at some temperature other than 30°.

3. Energy of Activation

From equation (16),

$$\log \frac{k_2}{k_1} = - \frac{E_a}{2.303R} \left(\frac{1}{T_2} - \frac{1}{T_1} \right),$$

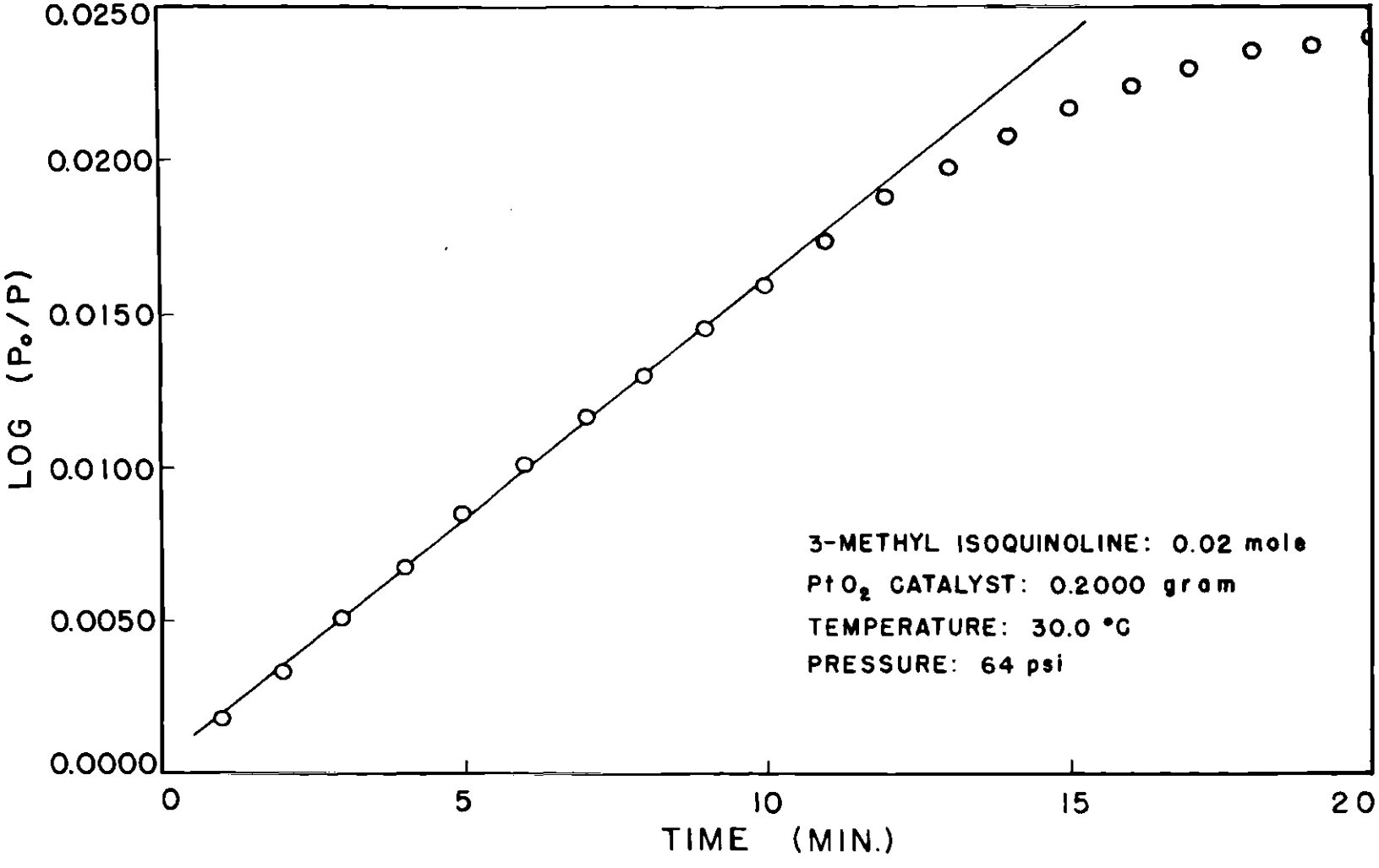

FIGURE 4

SAMPLE HYDROGENATION CURVE
FOR 3-METHYL ISOQUINOLINE

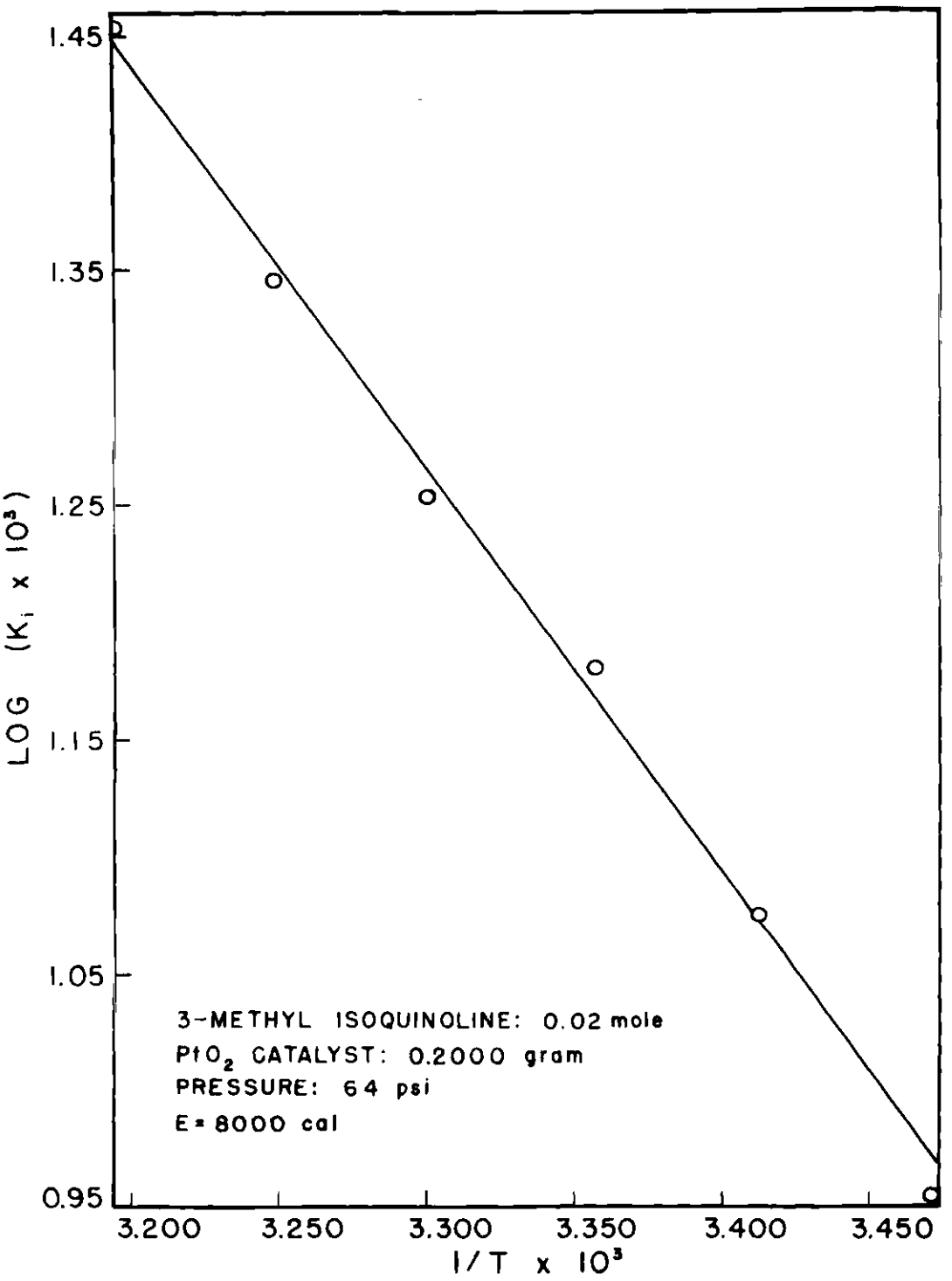

FIGURE 5

ENERGY OF ACTIVATION FOR THE HYDROGENATION OF 3-METHYL ISOQUINOLINE

derived on p. 11, there may be obtained the energy of activation, which may be used in correcting to temperatures other than that which a reaction is run. Figures 3 and 5 represent the results of such a determination for isoquinoline and 3-methylisoquinoline. The reaction rate constants were determined at the following temperatures: 15° C., 20° C., 25° C., 30° C., 35° C., and 40° C.; and, from a plot of log K_T vs. 1/T, there is obtained a straight line. The energy of activation may then be obtained by multiplying the slope of this line by -2.303R. For isoquinoline the energy of activation was found to be 7200 cal. per mole and that for 3-methylisoquinoline, 8000 cal. per mole. The energy of activation for 1,2,3,4-tetrahydroisoquinoline was not calculated because the reaction rate was too slow to have any real significance.

By means of either of these figures the rate constant at any one temperature may be corrected to another temperature, i.e., standard conditions, as long as it is in the range where the energy of activation is valid.

4. Sample Calculation.

From the data on the decrease in pressure with time, a plot, as shown in Figures 1,2, and 4, of the log p_o/p against time was made for each hydrogenation. Therefore from equation (10), p. 9, the rate constant could be calculated by multiplying the slope of the line by 2.303.

The reaction rate constant is then corrected to standard conditions--one gram of catalyst and benzoic acid standard.

The calculation for Figure 1 (Hydrogenation Number 53) is as follows:

Slope of line, m = 7.6×10^{-4}

(m) (2.303) =

$K_{30°/0.2000 \text{ gram catalyst}}$ = 17.5×10^{-4}

$K_{30°/\text{gram catalyst}} = K_{30°}$ = 87.5×10^{-4}

Catalyst Factor = 1.37

K^{o} = 119.9×10^{-4} min.^{-1} g.^{-1}

In a similar manner the K^{o} may be calculated for Figures 2 and 4.

B. FACTORS INFLUENCING THE RATE CONSTANT

The following factors and their effect upon the reaction rate constant have been studied: nature and amount of the hydrogen acceptor, the nature and amount of catalyst, and the initial hydrogen pressure.

1. The Nature and Concentration of Hydrogen Acceptor.

Although quinoline is hydrogenated to decahydroquinoline in a two-step procedure, this was definitely not the case with isoquinoline and 3-methylisoquinoline. After the addition of two moles of hydrogen these two organic compounds ceased to be hydrogenated. The apparatus was permitted to run in anticipation of further hydrogenation, as was the case in quinoline, but at the end of approximately four hours no reduction had taken place.

Another method used in attempting to reduce completely isoquinoline was as follows: after the addition of the calculated two moles of hydrogen, the reaction vessel was removed from the hydrogenation apparatus, the contents filtered to remove the spent catalyst, fresh catalyst was added, and the reaction vessel was again inserted into position. After a time interval of twelve hours, the same tetrahydroisoquinoline had been reduced, but the calculated amount of hydrogen to reduce the compound to decahydroisoquinoline had not been added. Since the rate of reduction was so slow, a kinetic study would have been impossible.

After the purification of the tetrahydroisoquinoline, as described on page 24, the compound could be hydrogenated to decahydroisoquinoline. The standard reaction rate constant for this reduction, as shown in Figure 2 was 23.0×10^{-4}, and since this is extremely small, a complete kinetic study was not made.

Varying concentrations of isoquinoline and 3-methylisoquinoline over a range of 0.01 mole to 0.04 mole were used in hydrogenations. As indicated in Tables I and II, p. 36, the rate constant for each hydrogen acceptor has been found to be zero order with respect to concentration as was also observed to be true in the case of benzoic acid and quinoline.

Check runs on the hydrogen acceptors, benzoic acid, isoquinoline, which was distilled in an atmosphere of nitrogen

TABLE I

Effect of Concentration of Isoquinoline

Using 0.2000 Gram of Catalyst (81.73%)

Hydrogenation Number	Concentration of Isoquinoline	$K^o \times 10^4$
33	0.01 mole	121
46	0.015 mole	118
53	0.02 mole	120
31	0.04 mole	119

TABLE II

Effect of Concentration of 3-Methylisoquinoline

Using 0.2000 Gram of Catalyst (81.73%)

Hydrogenation Number	Concentration of 3-Methylisoquinoline	$K^o \times 10^4$
68	0.01 mole	252
56	0.02 mole	243
65	0.04 mole	238

and kept in such an atmosphere, and 3-methylisoquinoline were made periodically throughout the investigation to determine if the value of the rate constant had altered. Any error noted was well within experimental error.

Since the rate constant doesn't change appreciably over the concentration range given, the hydrogen acceptors must be strongly adsorbed on the surface of the catalyst.

2. Nature and Amount of Catalyst.

Since dissimilarities in the chemical composition of platinum oxide catalysts have previously been noted, and, since these impurities affect the rate of reduction, a qualitative spectrographic analysis of the catalyst used in this investigation was made. The results of this analysis are outlined in Table III, p. 38.

In a hetergeneous reaction the action of a catalyst has been shown to be related directly to the surface area of the catalyst and to the active centers on the catalytic surface. Therefore, with sufficient hydrogen acceptor present, the rate of hydrogenation should increase proportionally as the amount of catalyst is increased. The results from varying the amount of catalyst in the range of 0.1 to 0.4 gram using 0.02 mole of hydrogen acceptor are given in Tables IV and V, p. 39.

The rate of hydrogenation for Hydrogenation Numbers 49 and 53, Table IV, were as predicted, directly proportional to

TABLE III

Qualitative Spectrographic Analysis of Catalyst[a]

Elements Found	Percent
Ca, Mg, Pd	0.01
Al, Fe, Mn, Pb, Rh	0.001
Co[b], As, Ag[c], Cr, Cu, Ir, Si, Th[b], Yb[b]	0.0001

a. Spectrogram for the catalyst sample was prepared by Peter B. Sherry, Georgia Institute of Technology.

b. This element is listed as doubtful.

c. These elements are present in an amount between 0.001% and 0.0001%.

TABLE IV

Effect of Amount of Catalyst on the Reaction Rate Constant Using 0.02 Mole of Isoquinoline

Hydrogenation Number	Amount of Catalyst	$K_{30°}$/ x gram x 10^4	K^o x 10^4
49	0.1000 gram	8.64	118
53	0.2000 gram	17.5	120
35	0.4000 gram	39.1	134

TABLE V

Effect of Amount of Catalyst on the Reaction Rate Constant Using 0.02 Mole of 3-Methylisoquinoline

Hydrogenation Number	Amount of Catalyst	$K_{30°}$/x gram x 10^4	K^o x 10^4
69	0.1000 gram	17.5	240
56	0.2000 gram	35.4	243
70	0.4000 gram	74.3	253

TABLE VI

Effect of Hydrogen Pressure on the Reaction Rate Constant Using 0.02 Mole of Isoquinoline and 0.2000 Gram of Catalyst

Hydrogenation Number	Initial Pressure (Corrected)	$K^{o} \times 10^{4}$
53	64.3 p.s.i.	120
58	32.6 p.s.i.	122
43	16.7 p.s.i.	124

the amount of catalyst; however, Hydrogenation Number 34 varies from that expected. This may possibly be explained from a poisoning standpoint. If any catalyst poison was introduced through the isoquinoline, reaction vessel, the acetic acid, or the hydrogen, the slowing influence would have greater effect on the calculated rate in the case of 0.1000 gram of catalyst than in larger quantities; whereas, in the larger quantities a more or less fixed amount of poison would be present.[2]

The rate constant was also found to be directly proportional to the amount of catalyst used in Hydrogenation Numbers 69 and 56, Table V. The slightly higher value for Hydrogenation Number 70 may be attributed to the same reason as that postulated for Hydrogenation Number 34.

3. Hydrogen Pressure.

As shown by Table VI, p. 40, the rate of hydrogenation has been found to be directly proportional to the hydrogen pressure. When the rate constant is calculated from the first order equation, it remains constant.

C. Products of Hydrogenation

On the addition of two moles of hydrogen to one mole of isoquinoline further hydrogenation did not occur. After the recovery of this product, which was discussed previously,

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[2]A. T. Trimble, "The Catalytic Hydrogenation of Quinoline," Master's Thesis, Georgia Institute of Technology, 1949.

it was identified as 1,2,3,4-tetrahydroisoquinoline by distillation and a picrate derivative. The portion distilling from 233.9° C. to 234.1° C. at 739 mm (corrected) was collected for further hydrogenation. The picrate derivative had a melting point from 195.5° C to 196.5° C. The melting point of the picrate is taken to be 195° C.

Upon further hydrogenation of the 1,2,3,4-tetrahydroisoquinoline, three moles of hydrogen were added to this compound to give decahydroisoquinoline. This product was recovered and found to distill from 207° C to 208° C at 739 mm (corrected). The boiling point is taken to be 207° C.

After the recovery of these compounds, 1,2,3,4-tetrahydroisoquinoline was obtained in an82.2% yield and the decahydroisoquinoline amounted to 85.6% from the 1,2,3,4-tetrahydroisoquinoline.

In a manner similar to isoquinoline, the hydrogenation of 3-methylisoquinoline stops upon the addition of two moles of hydrogen. Further hydrogenation of 3-methyltetrahydroisoquinoline was not attempted since it was anticipated that it would hydrogenate very slowly to 3-methyldecahydroisoquinoline, and a kinetic study would be impossible. Also, from distillation data it was decided that 3-methylisoquinoline hydrogenates to two compounds in the tetrahydro stage. One compound which was recovered in a 58.3% yield had a boiling point from 236.2° C to 237° C at 751 mm (uncorrected). Therefore, the fraction

obtained in a 58.3% yield may be said to be 3-methyl-1,2,3,4-tetrahydroisoquinoline. The other compound, which was obtained in a 25.3% yield is quite probably 3-methyl-5,6,7,8-tetrahydroisoquinoline.

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